ITC 4/52
Information Technology and Control
Vol. 52 / No. 4 / 2023
pp. 1073-1086
DOI 10.5755/j01.itc.52.4.34233

Chronic Kidney Disease Diagnosis Using Conditional Variational Generative Adversarial Networks and Squirrel Search Algorithm

Received 2023/05/28 | Accepted after revision 2023/09/08

HOW TO CITE: Brinda, M. B., Rajan, C. (2023). Chronic Kidney Disease Diagnosis Using Conditional Variational Generative Adversarial Networks and Squirrel Search Algorithm. *Information Technology and Control*, 52(4), 1073-1086. https://doi.org/10.5755/j01.itc.52.4.34233

Chronic Kidney Disease Diagnosis Using Conditional Variational Generative Adversarial Networks and Squirrel Search Algorithm

B. M. Brinda
Department of Computer Science Engineering, Paavai College of Engineering, Namakkal, 637018, India
C. Rajan
Department of Information Technology, K S Rangasamy College of Technology, Thiruchengode, 637 215, India

Corresponding author: bmbrindares1@outlook.com

Globally, chronic kidney disease (CKD) is steadily increasing. Computer-aided automated diagnostic (CAD) methods play a significant part in predicting CKD. Due to their highly effective classification accuracy, CAD systems like deep learning algorithms are essential in diagnosing diseases. This research creates an innovative categorization model with a metaheuristic algorithm based on the best characteristic selection to diagnose chronic kidney disease. Data with the absence of values were first removed during the pre-processing phase. Then, the optimal assortment of attributes is chosen using the Squirrel Search algorithm, a metaheuristic method that aids in more precise disorder prediction or categorization. Conditional Variational Generative Adversarial Networks were suggested for classification to identify the presence of CKD. A combination of two powerful techniques, Variational Autoencoders (VAEs) and Generative Adversarial Networks (GANs) are used. These networks can generate data based on specific conditions, making them well-suited for conditional generation tasks. Performance measures such as accuracy, precision, recall, and F1 score were evaluated on the benchmark CKD dataset to determine the efficiency of the suggested feature selection-based classifier. According to the experimental findings, the proposed method outperformed existing classification models with accuracy, precision, recall, and F1 score values of 99.2%, 98.4%, 98.6%, and 98.9%, respectively.

KEYWORDS: Chronic Kidney Disease, Deep Learning, Squirrel Search Algorithm, Generative Adversarial Networks.

1. Introduction

Chronic Kidney Disease (CKD) is a condition where kidney function gradually declines over time. It is a primary global health concern due to its increasing prevalence worldwide. CKD comprises a group of disorders that gradually damage the kidneys, reducing their ability to perform essential bodily functions over an extended period [5]. This condition can lead to kidney failure, high blood pressure, nerve damage, and other health issues. Estimates suggest that nearly two million people worldwide are affected by kidney failure, particularly in developing countries like Afghanistan, Bangladesh, Nepal, India, Sri Lanka, and Pakistan [21]. In the United States, CKD affects approximately seven million people each year. It is recommended that individuals with associated risk factors such as high cholesterol. Diabetes or a history of kidney disease should undergo regular annual check-ups to monitor abnormal test results [14]. Various laboratory tests, including measuring glomerular filtration rate and assessing protein levels in urine and blood, are commonly used for CKD diagnosis. These circumstances raise two significant concerns: the reliability of assessment tests and the increasing healthcare costs.

As those with End-Stage Renal Disease (ESRD) maintain their health through dialysis treatments such as hemodialysis, peritoneal, or a kidney transplant, early identification of CKD is essential and helpful in reducing medical resource usage [18]. Diagnostic tests employing plasma nitrogen levels and creatinine measurement are frequently used to diagnose CKD in its early stages. A technological way to diagnose CKD effectively is to analyze ultrasound scans of patients. Ultrasound imaging has several benefits, including the fact that it is safe, does not include radiation, is affordable, and is accessible [1]. Additionally, because the fatty deposits and collagen are farther down, ultrasonic imaging for obese individuals may have a lower accurate forecasting ratio and worse resolution. The precision of ultrasonics is primarily dependent on the technician's skills. However, the CT scan outcome provides a better-intensity image, making it easier to see the structure, dimension, and internal layout [15].

Electronic medical record systems, information gathered from insurance asserts, CT scan results, lab examination outcomes, and other data sets have all been produced due to the digitization of the medical sector [21]. The traditional healthcare system cannot efficiently and reliably diagnose CKD due to the enormous amount of accessible data. Thus, it is essential to undertake prospective healthcare analytics to leverage data [4]. Traditional healthcare administration has limitations, but predictive techniques like machine learning, deep learning models, and algorithms can help alleviate such constraints. Implementing Deep learning-based diagnosis may lessen the need for surgical operations and increase the effectiveness of current medical interventions [18].

Healthcare professionals may develop innovative solutions using advanced analytics to prompt CKD examination, related health concerns, and even recommendations for personalized treatment when they integrate this information with other data sources [5]. Early CKD identification can stop the progression of ESRD using Deep learning models. The feature selection technique may be used to overcome the constraint of dimensionality issues in categorizing the large dataset [15]. There are 2n alternative solutions for the FS selection issue with n features, and the difficulty increases by a factor of 2 for each additional feature. In recent studies, swarm intelligence (SI) algorithms have been chosen to handle FS since it is regarded as an NP-complete issue by selecting the best feature group [8, 25].

The primary motivation behind conducting this research is driven by the growing global prevalence of chronic kidney disease (CKD) and the need for accurate and efficient diagnostic methods. As CKD becomes increasingly common, developing reliable tools for early detection and categorization of the disease has become essential. Traditional diagnostic procedures may be unable to keep up with the rising demand, making it crucial to explore innovative approaches to improve the accuracy and efficiency of CKD diagnosis. There is a need for advanced diagnostic methods that can help healthcare professionals identify and categorize CKD cases accurately and efficiently. Deep learning can learn complex patterns and features from medical data. They can reveal subtle indicators of CKD that are difficult for human observers to detect. The research aims to create an innovative categorization model that improves the accuracy of

CKD diagnosis. This innovation is driven by recognizing existing methods' limitations and the desire to push the boundaries of what is possible in disease classification.

To address these problems, a novel classification model for the diagnosis of CKD based on Feature Selection is provided in the present research. Data with values that were unavailable were first removed during the pre-processing phase. Then, the optimal collection of characteristics was chosen using a metaheuristic method called Squirrel Search Algorithm (SSA), which is based on the concept of flying squirrels' behavior. The optimal supply of features chosen by this metaheuristic optimization process aids in more precise disease prognosis or categorization. Conditional Variational Generative Adversarial Networks (CVGAN) have been suggested as a classification method to determine the presence of chronic kidney disease. A series of tests were run on the benchmark CKD dataset to evaluate the performance of the recommended model.

The main contributions of this work are,

1 To propose a novel deep learning model, such as a Conditional Variational Generative Adversarial Network for categorizing Chronic Kidney disease.
2 To employ a recently developed Squirrel Search Algorithm to select the most optimal features from the benchmark CKD dataset to improve the efficacy of the classification performed by the CVGAN deep learning model.
3 To assess the performance of the proposed model by comparing it against conventional deep learning models with and without feature selection techniques and further compare the proposed model with existing works from the literature to demonstrate its performance supremacy.

The remainder of the paper is organized as follows. Section 2 discusses the existing works in the literature associated with chronic kidney disease classification incorporating Machine Learning and Deep Learning models. Section 3 describes the proposed methodology, which includes the preprocessing phase and a brief description of CVGAN and SSA techniques. Section 4 presents the results of executing experiments using the CVGAN-SSA model by applying it to the CKD dataset. Section 5 concludes the present research.

2. Related Works

It is apparent from a review of the published works that researchers are now primarily interested in diagnosing CKD. The investigations strongly emphasized using Machine Learning and Deep Learning algorithms. However, researchers have recently been interested in deep learning models because of their widespread adoption.

Kidney diseases are diagnosed using 14 ML techniques with an ensemble model [7]. Here, the 13 types of input features are used, such as diastolic BP, specific gravity, Albumin, Glucose, RBC, blood urea, serum, sodium, hemoglobin, potassium, hypertension, CKD, and blood counts. The Bayesian network, SVM, random forest, rotation forest, logistic regression, decision tree, Naive Bayes, KNN, Logistic model tree, J48, and Ada Boost models were re-tested with the above input features. The voting and stacking are used to ensemble the high probability outcome and analyze the performance of the model.

Ten ML algorithms [5] are applied to construct prediction models, incorporating 19 demographic, medical history, behavioral, and biochemical features. The study employs three feature ranking techniques to assess the significance of each feature. This research leverages ML algorithms to address a crucial healthcare challenge by providing a method for the early prediction of CKD in T1DM patients using readily available clinical data. The findings suggest that RF and LightGBM are promising models for this task, potentially improving CKD diagnosis and intervention in this high-risk patient population.

The study [6] utilizes a substantial dataset comprising sixteen years of longitudinal data from 1375 T1DM patients gathered from the multi-center Epidemiology of Diabetes Interventions and Complications (EDIC) clinical trials conducted across the USA and Canada. Seventeen routinely available features are considered. Three feature ranking algorithms, including extreme gradient boosting (XGB), random forest (RF), and extremely randomized trees classifier (ERT), are employed to create ranked feature lists. Logistic regression analyses are then conducted to construct CKD prediction models based on these rated features. Eight top-ranked features, including hypertension, duration of diabetes, drinking habit, triglycerides, ACE inhibitors, low-density lipoprotein

(LDL) cholesterol, age, and smoking habit, are identified as the most critical for predicting CKD in T1DM patients. A multivariate logistic regression-based CKD prediction model is developed using these features, achieving a high accuracy of 90.04% in internal data validation and 88.59% in test data validation. The proposed model exhibits excellent performance and offers a practical solution for identifying CKD in T1DM patients during routine checkups. Including a nomogram further enhances the applicability of the model in clinical practice, making it a valuable tool for early CKD detection in this at-risk patient population.

The potential of Computer-aided automated diagnostic (CAD) systems is profound learning algorithms in enhancing CKD prediction due to their high classification accuracy. The study explores the application of seven state-of-the-art deep learning algorithms to predict and classify CKD using various clinical features [1]. The research meticulously evaluates the performance of these algorithms, measuring accuracy, precision, recall, loss, validation loss, computation time, prediction ratio, and AUC. Notably, algorithms such as ANN, Simple RNN, and MLP achieve high accuracy levels of 99%, 96%, and 97%, respectively, along with efficient prediction ratios and reduced processing time. These deep learning models outperform traditional data classification techniques, offering superior predictive capabilities. Moreover, the article proposes integrating the best-performing deep learning models into the Internet of Medical Things (IoMT) to enhance CKD prediction through more efficient and effective deep learning methods. This integration is envisioned to advance predictive analytics for CKD while considering its associated risk factors.

The primary objective of the research [30] is to predict and classify CKD using ML approaches, leveraging a publicly available dataset from the Irvine ML Repository comprising 400 instances. Various ML methods, including Support Vector Machine (SVM), K-Nearest Neighbors (KNN), Random Forest (RF), Logistic Regression (LR), Decision Tree (DT) Classifiers, and eXtreme Gradient Boosting (XGBoost), are employed as base learners.

The research [28] focuses on developing a machine-learning model for forecasting CKD occurrence using publicly available data. The process involves comprehensive data preprocessing steps, including imputation of missing data, data balancing using the SMOTE algorithm, and feature scaling. The study employs the chi-squared test to extract a minimal set of relevant and highly correlated features for prediction. Multiple machine learning models [25] are implemented, including decision tree (DT), random forest, and multi-class AdaBoosted DTs. The study focuses on improving the early prediction of CKD, particularly in the context of imbalanced and limited-size datasets, a common issue in medical research. Through rigorous analysis using various validation techniques [4], such as hold-out validation, multiple stratified cross-validation, and nested cross-validation, the DT model emerges as the top performer, achieving a high accuracy score of 98.99% when using manual augmentation and SMOTE.

A severe and long-lasting ailment that can be caused by factors such as kidney malfunction or malignancy is discussed [13]. The study emphasizes the importance of early detection and intervention to slow or halt the progression of CKD, potentially preventing the need for life-preserving interventions like dialysis or surgery. The research [12] explores the prediction of CKD using various machine learning models, including logistic regression, probit, random forest, decision tree, k-nearest neighbor, and support vector machine (SVM) with four different kernel functions. The dataset is derived from a case-control study involving CKD patients from a specific region in Pakistan. Multiple performance measures, such as accuracy, Brier score, sensitivity, Youden's index, specificity, and F1 score, with additional the Diebold and Mariano test is conducted to assess

The article [17] addresses a significant challenge in pathology related to chronic kidney disease (CKD) diagnosis through kidney biopsy samples. Traditional visual classification methods used by pathologists are qualitative, semi-quantitative at best, and suffer from substantial interobserver variability. The study introduces an innovative approach using unsupervised machine learning to overcome these limitations and discover predictive features for patient outcomes. The study [21] proposes a Deep Neural Network-based Multi-Layer Perceptron Classifier for CKD diagnosis. The model is trained using data from 400 individuals, considering various symptoms and signs, including age, blood sugar, and red blood cell count. The study [32] analyzed data from 1263

CKD patients and 1948 non-CKD patients admitted to a hospital over ten years. Various machine learning algorithms were employed to create prediction models, including XGBoost, random forest, Naive Bayes, support vector machine, and multivariate logistic regression. Additionally, the study introduced a new MD-BERT-LGBM model to process unstructured data and compared its performance with structured data models.

The article [33] addresses the significant global health problem of chronic kidney disease (CKD) and aims to identify critical biomarkers and develop an integrated model for the early prediction of CKD. The research leverages existing RNA-seq data and clinical information from CKD patients from the Gene Expression Omnibus (GEO) database. A computational approach combines the random forest (RF) and artificial neural network (ANN) methodologies for gene biomarker identification and model construction. The article [22] discusses the application of machine learning algorithms (MLAs) in predicting early chronic kidney disease (CKD) and its progression [29]. The primary aim is to review existing publications on this topic to understand the potential of MLAs in improving the diagnosis and management of CKD.

The use of machine learning to predict the risk of end-stage renal disease (ESRD) in sepsis survivors who also have chronic kidney disease (CKD) is discussed [18]. The main goal is to predict the risk of ESRD development in patients who survive sepsis and have CKD. It utilizes a machine learning approach to analyze a dataset of sepsis survivors and CKD patients to build a predictive model. The study includes 11,661 sepsis survivors from a database of 112,628 CKD patients, with a follow-up period of approximately 3.5 years. Various machine learning algorithms, including random forest, extra trees, extreme gradient boosting, light gradient boosting machine (LGBM), and gradient boosting decision tree (GBDT), were employed to predict the risk of ESRD development.

Chronic Kidney Disease (CKD) is a significant issue proposing a novel hybrid approach for diagnosing the disease and predicting its progression [23]. A filter-based system using the ReliefF method to assign weights and ranks to each feature in the dataset. Dimensionality reduction using Principal Component Analysis (PCA) to extract the most informative subset of features. To enhance processing speed, the research employs simultaneous execution on multiple processors. The performance of ML algorithms in detecting CKD is reviewed [20] wisely. The study [26] preprocesses the data by replacing missing values with the average associated features of the database. The optimal parameters of the deep neural network model are determined through multiple trials. Recursive Feature Elimination (RFE) is used to select the most important features for classification. Key features selected by RFE include Hemoglobin, Specific Gravity, Serum Creatinine, Red Blood Cell Count, Albumin, Packed Cell Volume, and Hypertension. The set features are then passed to various machine learning classifiers for comparison.

The study [16] utilizes data from the National Health and Nutrition Examination Survey (NHANES) in the USA from 1999 to 2012. Insulin resistance is assessed using the homeostasis model assessment of IR (HOMA-IR). ML algorithms, including random forest (RF), eXtreme Gradient Boosting (XGBoost), logistic regression, and deep neural learning (DNN), are employed to build predictive models.

It is evident from the analysis of the existing works on CKD that machine-learning algorithms have been employed extensively for the classification of renal disease. A limited amount of research is leveraging advanced deep-learning models for CKD classification. Additionally, feature selection algorithms are also used scarcely with deep learning models to select the maximally optimal features. Hence, this research is motivated to develop a unique deep learning-based model by integrating it with a metaheuristic optimization algorithm to choose the best characteristics from the dataset to improve the precision of the classification.

3. Proposed Methodology

This section elaborates on the proposed methodology, including preprocessing, feature selection, and classification phases. The preprocessing stage was used to analyze the dataset to find and remove the missing values. Also, the conversion of categorical to numerical values was executed. Feature selection is performed using the Squirrel Search algorithm, which selects the most optimal features from the original CKD dataset. CVGAN model is used to accomplish

the classification tasks to identify whether the individual is affected by CKD or not. Further, the performance of the proposed model was also assessed using various metrics. The workflow of the proposed methodology is depicted in Figure 1.

3.1. Preprocessing

The legitimate CKD healthcare dataset from the UCI machine learning repository was considered for the disease detection in the proposed work. Certifiable archives sometimes include inaccurate data impotent against noise and are occasionally missing. This is due to their frequently enormous size and different points of origin. Pre-processing must be considered while classifying CKD data to improve the data quality used in the extraction procedure. This procedure is used to exclude unnecessary data from the healthcare dataset. Preprocessing is therefore required to increase the reliability of predictions while maintaining the integrity of the data.

Using deep learning, the absence of information in the healthcare information set might pose a concern. Each character in the medical data is typically thought to influence how one would rate one's health substantially. Therefore, the method used to transform the unprocessed information into a dataset free from errors is known as data pre-processing. The fundamental stage of every DL model or classifier method is training. Preprocessing was done by turning categorical text data columns into flat numeric data columns. There are two possible definitions for categorical numerical data: 0 (negative statement) and 1 (positive statement).

To fill up the missing variables, imputations with multiple values were used. The interpolation method was based on logistic regression for categorical data and linear regression for continuous variables. It preserves the statistical properties of the data, which can be necessary for downstream analyses and modeling. Numerous aspersions replace missing values in the dataset n times, where n is often a low number between 3 and 10. To create ten separate datasets, we used numerous imputations for ten iterations. We selected the dataset with the variables' averages and standard deviations closest to those of the original dataset to reduce the data to a subset with a realistic range of values. The missing values for the complete set of data were then filled in.

3.2. Squirrel Search Algorithm

When flying squirrels start their scavenging, the search for food process commences. The squirrels jump from one tree to another for food supplies during the warm months of the year. They ingest acorns as soon as they come across them because the climate is sufficiently hot for them to satisfy their daily energy demands more rapidly on a diet of plentiful acorns. After obtaining their daily energy needs, they begin looking for the best food source for the winter: hickory nuts. Hickory nut storage will help them meet their energy needs in harsh weather, cut down on expensive scavenging journeys, and boost the likelihood of survival. Flying squirrel activity resumes after the completion of the winter season. This continuous cycle lasts until a squirrel's lifetime and is the basic idea for the Squirrel Search algorithm.

Like any other population-based algorithm, the Squirrel Search algorithm starts with an initial set of populations with K squirrels. The starting position of the squirrel in the forest is represented through (1)

$$SQ_k = SQ_{lower} + R(0,1) \times (SQ_{upper} - SQ_{lower}), \quad (1)$$

where SQ_{lower} and SQ_{upper} are the higher and lower limits of the squirrels with $R(0,1)$ representing a random number between 0 and 1.

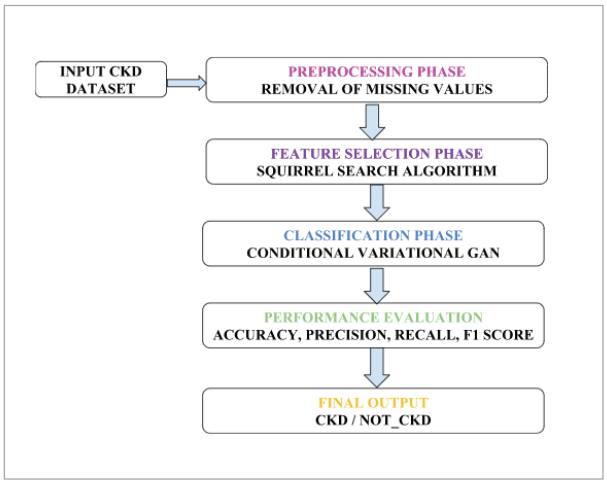
The fitness function of the squirrels in motion is denoted using (2),

$$FF = func(SQ_1, SQ_2, ...SQ_k). \quad (2)$$

A flying squirrel with low fitness value has been reported on the hickory nut tree. The following three top flying squirrels are thought to be on acorn nut trees and are anticipated to migrate to hickory nut trees. It is expected that the surviving flying squirrels will be on typical trees. More randomly, it is assumed that some squirrels would walk towards the hickory nut tree after consuming their daily energy needs. The surviving squirrels will visit Acorn nut trees. The presence of attackers constantly affects the flying squirrel's foraging habits. The location refresh strategy, along with the possibility of an attacker present, is used to represent this natural behavior.

If an attacker is not present, the squirrel flies effortlessly explores the forest for its preferred meal, but

Figure 1
Proposed CV-GAN work flow model



when an attacker is present, it becomes wary and must take short, unplanned excursions to look for a hiding place. The location refresh strategy of squirrels are denoted in (3) to (5). Equation (3) represents the motion of the squirrels from acorn nut trees to hickory nut trees.

$$SQ_{xd}^{d+1} = SQ_{xd}^{d} + c_m \times M_{ct} \times (SQ_{yd}^{d} - SQ_{xd}^{d}) V_1 \geq AE_{prob}, \quad (3)$$

where c_m is the distance moved by the squirrel, V_1 is an arbitrary number between 0 and 1, SQ_{xd}^{d} denotes the position of squirrel on acorn nut tree and SQ_{yd}^{d} denotes the position of squirrels on hickory nut trees. M_{ct} is a constant value with respect to the motion of the squirrel. AE_{prob} denotes the attacker's existence probability whose value is set to 0.1.

The location update in case of movement of the squirrel from ordinary trees to acorn nut in search of food is represented in (4),

$$SQ_{zd}^{d+1} = SQ_{zd}^{d} + c_m \times M_{ct} \times (SQ_{zd}^{d} - SQ_{z_z}^{d}) V_2 \geq AE_{prob}, \quad (4)$$

where V_2 is an arbitrary number between 0 and 1. SQ_{zd}^{d} denotes the position of squirrels on ordinary trees. The other possible case of location update happens when squirrels that are present on regular trees after eating acorn nuts move in search of hickory nut trees to save food for the winter season and is shown in (5),

$$SQ_{zd}^{d+1} = SQ_{zd}^{d} + c_m \times M_{ct} \times (SQ_{zd}^{d} - SQ_{z_z}^{d}) V_3 \geq AE_{prob}. \quad (5)$$

The value of c_m which is the distance moved by the squirrel is determined using the formulation shown in (6),

$$c_m = \frac{l_m}{\tan\theta}, \quad (6)$$

where l_m denotes the loss incurred in the distance due to the movement of squirrels. θ denotes the angle at which the squirrel descends when it moves from one location to another.

Seasonal variations have a big impact on how squirrels graze. Owing to their tiny size, elevated temperature levels, and perilous feeding, they lose a large amount of heat at low temperatures. Compared to autumn, climatic factors make them less active in winter. As a result, weather changes impact squirrel movement, and accounting for this behavior may result in a more rational strategy to optimization. The seasonal tracking constraint is formulated as $H_{cs} < H_{min}$. The value of H_{cs} is computed using (7) and H_{min} is determined using (8) as follows.

$$H_{cs} = \sqrt{\sum_{i=1}^{c} (SQ_{xd,i}^{d} - SQ_{yd,i})^2} \quad (7)$$

$$H_{\min} = \frac{10E^{-6}}{(364)^{S/(S_i/2.5)}}, \quad (8)$$

where s and s_i are the present and highest values of iterations correspondingly.

After the winter season, the squirrels change their locations as per the representation in (14),

$$SQ_{zd}^{new} = SQ_{lower} + Levy(k) \times (SQ_{upper} - SQ_{lower}) \quad (9)$$

Where $Levy(k)$ denotes the Levy distribution, which helps for effective search. Researchers apply Levy flight, a potent mathematical technique, to enhance the overall discovery capabilities of several meta-heuristic algorithms. Levy flights aid in the identification of new potential solutions that are distant from the most effective one currently available. Figure 2 depicts the steps involved in the Squirrel Search algorithm.

Algorithm 1. Squirrel Search algorithm

Input: Initial population of k squirrels

Output: SQ_{yd}^{d} squirrel location on hickory nut tree

Step 1: Set locations of squirrels as SQ_{xd}^{d}, SQ_{yd}^{d}, SQ_{yd}^{d} denoting the squirrels on acorn nut trees, hickory nut trees and ordinary trees, respectively

Step 2: Compute the survival function for the squirrels

Step 3: Arrange the squirrels based on the survival rate of squirrels

Step 4: Initialize the locations of squirrels randomly on acorn nut trees, hickory nut trees and ordinary trees

Step 5: for s=1 to k1 (represents the motion of the squirrels from acorn nut trees to hickory nut trees)

Step 6: if $V_1 \geq AE_{prob}$

Step 7: $SQ_{xd}^{d+1} = SQ_{xd}^{d} + c_m \times M_{ct} \times (SQ_{yd}^{d} - SQ_{xd}^{d})$

Step 8: else

Step 9: SQ_{xd}^{d+1} = arbitrary location

Step 10: for s=1 to k2 (represents movement of the squirrel from ordinary trees to acorn nut in search of food)

Step 11: if $V_2 \geq AE_{prob}$

Step 12: $SQ_{zd}^{d+1} = SQ_{zd}^{d} + c_m \times M_{ct} \times (SQ_{xd}^{d} - SQ_{zd}^{d})$

Step 13: else

Step 14: SQ_{zd}^{d+1} = arbitrary location

Step 15: for s=1 to k3 (represents the movement of the squirrel from ordinary trees to hickory nut trees)

Step 16: if $V_3 \geq AE_{prob}$

Step 17: $SQ_{zd}^{d+1} = SQ_{zd}^{d} + c_m \times M_{ct} \times (SQ_{yd}^{d} - SQ_{zd}^{d})$

Step 18: else

Step 19: SQ_{zd}^{d+1} = arbitrary location

Step 20: Calculate seasonal constraint H_{cs} as per (7)

Step 21: Determine minimum seasonal constraint H_{min} as per (8)

Step 21: if $(H_{cs} < H_{\min})$

Step 22: Relocate the squirrels as per (9)

Step 23: return to the optimal location of the squirrel, SQ_{yd}^{d}

3.3. Conditional Variational Generative Adversarial Networks

This section describes the CVGAN model for performing classification. The first component in the CVGAN model is the encoder, which maps the input to its appropriate representation according to the category to which the data belongs. The loss incurred during this process is denoted as in (9),

$$En_{loss} = \frac{1}{2}\left(-\log\phi^2 + \delta^2 + \phi^2 - 1\right), \quad (9)$$

where ϕ and δ represents the average and skewness of the output that is produced by the encoder.

The second component in the CVGAN model is the generator network, which produces data distributed over the complete set of samples. This network produces data by distributing information from the third component, the discriminator. This discriminator network is responsible for differentiating between positive or negative samples in the data, and its loss is formulated as in (10),

$$DC_{loss} = -En_a[\log DC(a)] - En_c[\log(1 - Dc(Gn(c)))], \quad (10)$$

where a is the input to the encoder network with the distribution of samples denoted as c.

The generator network employs a function for mapping the attributes according to the optimal solution. The characteristic distribution centers of the fake specimens must coincide with the characteristic distribution centers of authentic samples to enable the target function to work. The loss function reduced by the generator network concerning the discriminator is represented in (11),

$$GnDc_{loss} = \frac{1}{2}\left\| En_a Dc_f(a) - En_c Dc_f(Gn(c)) \right\|_2^2, \quad (11)$$

where Dc_f denotes the attributes passed on to the hidden layers in the network.

Further, the target function is mapped by using the mean value of the attributes and the loss reduced concerning the classifier is represented as in (12),

$$GnCl_{loss} = \frac{1}{2}\sum_{b}^{B}\left\| En_a Cl_f(a) - En_c Cl_f(Gn(c,b)) \right\|_2^2, \quad (12)$$

where CL_f denotes the outputs of the hidden layers and b is the target labels for the corresponding input a. The cumulative generator loss is shown in (13),

$$Gn_{loss} = \frac{1}{2}\left(\left\|a - a'\right\|_2^2 + \left\|DC_f(a) - DC_f(a')\right\|_2^2 + \left\|Cl_f(a) - Cl_f(a')\right\|_2^2\right), \quad (13)$$

where a and a' denote the input data and the data produced by the generator network.

The fourth component, which is the classifier, takes a' as input and generates the output, which is decoded to value based on probability using the softmax function. The loss of the classifier network is reduced using (14),

$$Cl_{loss} = -En_a[\log P(b \mid a')]. \quad (14)$$

The aggregate loss of the CVGAN model is represented as shown in (15),

$$Agg_{loss} = En_{loss} + Gn_{loss} + GnDc_{loss} + GnCl_{loss} - Dc_{loss} + Cl_{loss}. \quad (15)$$

The target functions of all four components in the CVGAN model complement one another and finally aid the algorithm to produce the best outcomes.

4. Results

4.1. Dataset Description

The experiments were implemented using Python 3.10.11 by applying the proposed model to the CKD dataset. The dataset can be accessed using the given link:

https://archive.ics.uci.edu/ml/datasets/chronic_kidney_disease

The CKD dataset is composed of samples counting to 400 with 25 characteristics. Two class labels finally provide whether the individual is affected by CKD or NOT_CKD. Among the 400 samples in the dataset, 250 belong to the CKD target class and 150 belong to the NOT_CKD target class.

4.2. Experimental Results

The performance of the proposed CVGAN-SSA model is evaluated using standard metrics used for classification, such as Accuracy, Precision, Recall, and F1-Score. Initially, the classification technique CVGAN is applied to the entire dataset containing all the features without using the SSA technique for feature selection, and the results are obtained. Further, SSA is used for selecting optimal features and then classification is performed again using CVGAN. The results produced by the proposed model with and without the feature selection technique are compared against conventional deep learning models to comprehend the performance superiority of the CVGAN classification technique. Table 2 summarizes the results of traditional deep learning models and the proposed CVGAN model.

Table 2
Comparison of traditional DL models and proposed model without feature selection

Model	Accuracy (%)	Precision (%)	Recall (%)	F1 Score (%)
DNN	88.5	87.4	87.8	88.1
LSTM	89.2	88.1	88.4	88.9
SAE	90.3	89.2	89.6	90.1
MLP	91.5	90.5	90.9	91.2
RBFN	93.7	92.5	92.8	93.2
Bi-GRU	95.6	94.1	94.5	95.2
CVGAN	97.5	96.8	97.1	97.3

The traditional deep learning models taken for comparison purposes include Deep Neural Networks (DNN), Long short-term Term Memory Networks (LSTM), Stacked Autoencoders (SAE), Multilayer Perceptron (MLP), Radial Basis Function Networks (RBFN) and Bi-directional Gated Recurrent Units (Bi-GRU). The experiments are conducted on the CKD dataset utilizing these models and the results are obtained without a feature selection process. The accuracy of DNN is 88.5%, LSTM is 89.2%, SAE is 90.3%, MLP is 91.5%, RBFN is 93.7%, Bi-GRU is 95.6%, and the proposed CVGAN model for chronic kidney disease prediction produces an accuracy of 97.5% which is the highest among all the models. Similarly, for the other metrics, such as Precision, Recall, and F1 Score, the proposed model exhibits higher values than the other deep learning models. Further, the Squirrel Search Algorithm is applied to extract optimal features from the CKD dataset. These selected features are passed on to the classification model. The characteristics such as age, bp, al, su, rbc, bgr, bu, sc, hemo, wbcc, rbcc, htn, and dm are selected by the SSA technique from the CKD dataset. The extracted features are presented in Table 3. We have run 100 epochs for two iterations with an accuracy of 97.3%. The actual affected and predicted results are used to calculate the accuracy, precision, and recall.

Figure 4
Performance Comparison of classification techniques without feature selection

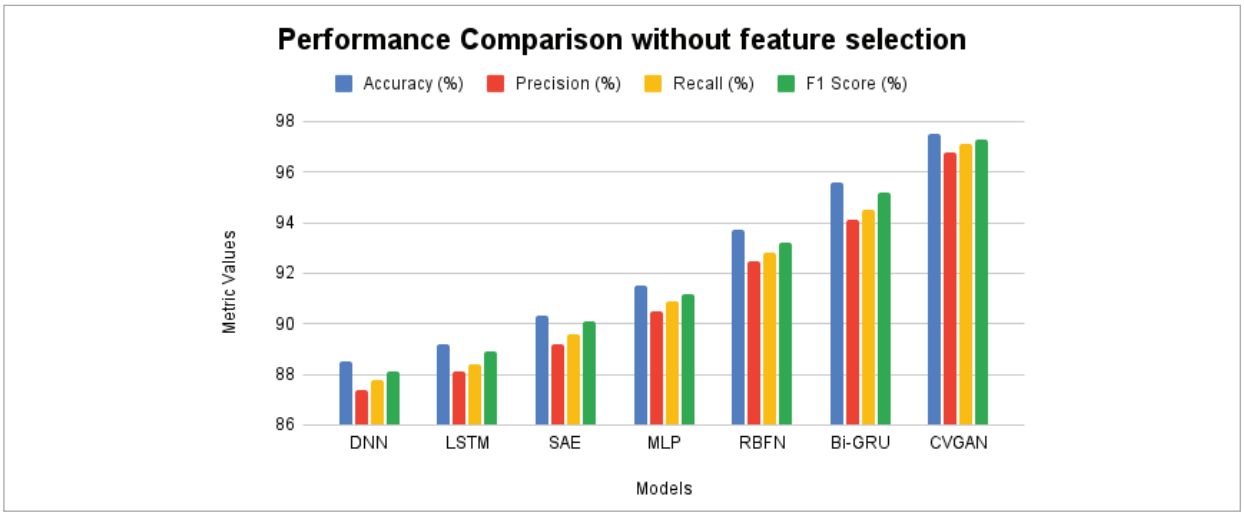


Table 3
Selected Features using SSA technique

Feature No.	Feature Name
F1	age-Age
F2	bp-Blood Pressure
F4	al-Albumin
F5	su-Sugar
F6	rbc-Red Blood Cells
F10	bgr-Blood Glucose Random
F11	bu-Blood Urea
F12	sc-Serum Creatinine
F15	hemo-hemoglobin
F17	wbcc-White Blood Cell Count
F18	rbcc-Red Blood Cell Count
F19	htn-Hypertension
F20	dm-Diabetes Mellitus
F25	Class- Target Class

The results achieved after applying the deep learning models and the proposed model to the selected features using the SSA technique are shown in Table 4. It can be noted that there is an improvement in the performance of the models after utilizing the feature selection algorithm. The accuracy of the DNN model is increased to 90.5%, precision is improved to 89.9%, recall to 90.1% and F1 Score is 90.3%. The accuracy of LSTM, SAE, MLP, RBFN, and Bi-GRU are enhanced as 91.8%, 92.6%, 93.7%, 95.6%, and 97.8%, respectively. Similar to accuracy, the precision, recall, and F1 score values also increase on employing the feature selection. However, the proposed model produces the highest accuracy, precision, recall, and F1 score values at 99.2%, 98.4%, 98.6%, and 98.9%, correspondingly.

Table 4
Comparison of traditional DL models and proposed model with selected features

Model	Accuracy (%)	Precision (%)	Recall (%)	F1 Score (%)
DNN	90.5	89.9	90.1	90.3
LSTM	91.8	90.7	91.2	91.5
SAE	92.6	91.6	92.1	92.2
MLP	93.7	92.4	92.8	93.3
RBFN	95.6	94.2	94.7	95.3
Bi-GRU	97.8	96.4	96.8	97.3
CVGAN	99.2	98.4	98.6	98.9

In addition to this, the performance of the proposed CVGAN-SSA model is also compared with the existing methods in the literature, such as Residual

Figure 5
Performance Comparison of classification techniques with feature selection SSA

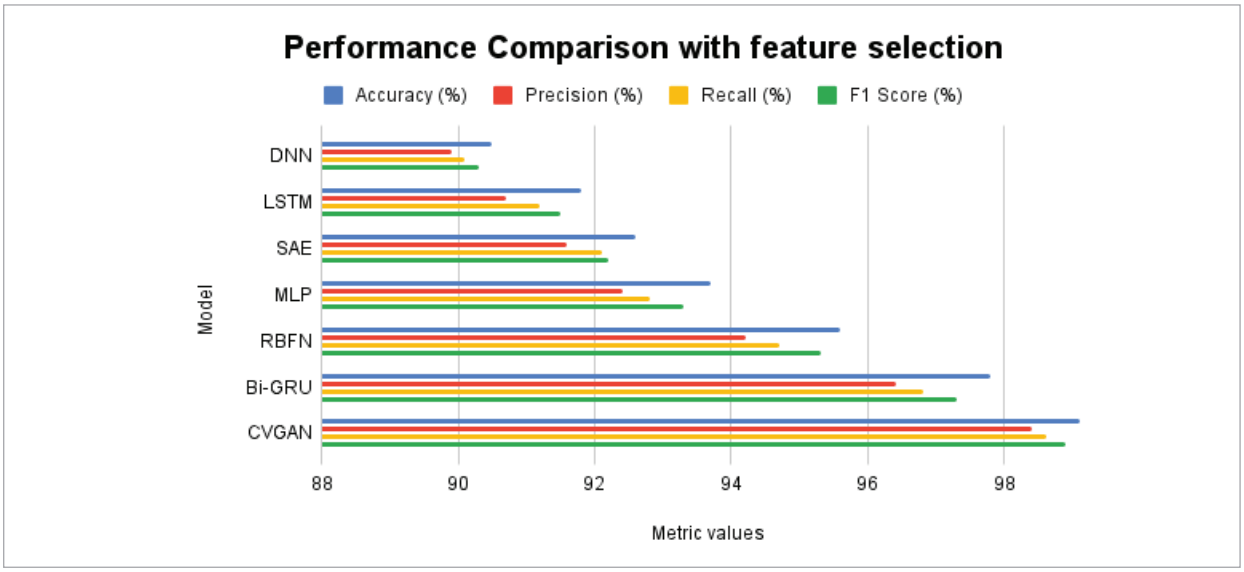


Table 5
Comparison of existing models and proposed model

Model	Accuracy (%)	Precision (%)	Recall (%)	F1 Score (%)
RDA-UNET [23]	-	96.34	96.88	-
OFFO-DNN [3]	98.89	-	-	-
MKSVM-FFO [2]	98.5	-	-	-
EDL-CDSS [9]	96.91	-	-	96.92
HMANN [10]	97.5	-	-	-
Proposed - CVGAN-SSA	99.2	98.4	98.6	98.9

dual-attention module with UNet (RDA-UNET), Oppositional based FireFly Optimization with Deep Neural Network (OFFO-DNN), MultiKernel SVM with FruitFly Optimization algorithm (MKSVM-FFO), Ensemble of deep learning based clinical decision support systems (EDL-CDSS) and Heterogeneous Modified Artificial NeuralNetwork (HMANN). The RDA-UNET model offers precision and recall values of 96.34% and 96.88%, respectively. OFFO-DNN produces an accuracy of 98.89% in classifying chronic renal disease effectively, while the MKSVM-FFO combination exhibits an accuracy of 98.5%. The EDL-CDSS model is 96.91% accurate in categorizing kidney disease, with an F1 score of 96.92%. Table 5 presents a comparison between the existing models and the proposed model. The HMANN model, which incorporates a Support Vector Machine and multilayer Perceptron with a Backpropagation technique, produces an accuracy of 97.5%. Compared to the existing models in the literature, the proposed CVGAN-SSO has a superior accuracy of 99.2%, precision of 98.4%, recall of 98.6% and F1 Score of 98.9%.

The proposed model, CVGAN-SSA, has the highest accuracy (99.2%) compared to all the existing models (RDA-UNET, OFFO-DNN, MKSVM-FFO, EDL-CDSS, and HMANN). This suggests that the CVGAN-SSA model performs exceptionally well regarding overall prediction accuracy.

The proposed model has a precision of 98.4% and a recall of 98.6%. The proposed precision and recall values of the model indicate its ability to make accurate positive predictions (high precision) and correctly identify positive cases (high recall). The F1 score, which balances precision and recall, has yet to be reported for several models. However, the proposed CVGAN-SSA model achieves an F1 score of 98.9%, indicating a solid balance between precision and recall, making it a well-rounded model. Drawing specific conclusions without detailed information on the training data, validation process, and specific tasks is challenging. However, the table suggests that the proposed

CVGAN-SSA model outperforms the other models in terms of accuracy, precision, recall, and F1 score, demonstrating its superiority in this comparison.

4.3. Discussion

Deep learning techniques like C-VGANs have demonstrated remarkable predictive power in various domains. Their ability to learn complex patterns in data makes them attractive for medical diagnosis tasks, including CKD prediction. The Squirrel Search algorithm offers a metaheuristic approach to feature selection. It aims to find the optimal attributes that contribute the most to the classification task. This automated feature selection process is crucial in improving model efficiency and reducing the risk of overfitting.

C-VGANs are well-suited for conditional generation tasks. In the context of CKD diagnosis, the model can generate data based on specific conditions, allowing it to identify the presence of CKD under various scenarios. This adaptability is essential when dealing with complex medical data.

The combination of advanced feature selection (Squirrel Search) and deep learning (C-VGANs) is relatively novel and innovative. This research likely pushes the boundaries of CKD diagnosis by leveraging the strengths of both techniques.

4.4. Limitations of Current Research

The results might need to be revised since the dataset is tiny. Finding a dataset with more characteristics and higher occurrences is challenging. The dynamic acquisition of information from the Internet of Medical Things platform is even more difficult. However, overfitting was avoided during optimization by adjusting the parameters used to quantify the difference in variance between the training and test datasets. Several input layers, hidden layers, and optimizers were effectively implemented in this research. Thus, despite having 400 records, it can be claimed that the models were balanced with training data.

5. Conclusion

The present research investigated the classification of health-related data to quickly identify the patient's illness. Evaluating the optimal subset of attributes from many characteristics of the CKD dataset is a crucial problem in health-related data classification. The suggested Squirrel Search algorithm was used to choose the best features after the data traversed a preliminary processing step in which values that were not present were eliminated. Based on the best subset of characteristics, the classification was performed to identify the existence and nonexistence of CKD. The CVGAN approach was used for performing the classification tasks. On CKD datasets, the performance parameters such as precision, recall, F1 score, and accuracy reached their maximum value using CVGAN. According to the findings, the suggested CVGAN-SSA produced promising classification results of 99.2% accuracy compared to other existing methodologies. Innovative algorithms or prediction approaches may be added for CKD diagnosis, and new extraction techniques may be utilized to eliminate missing information. Developing cutting-edge and composite optimization techniques for identifying features and healthcare data categorization can be considered the focus of future efforts.

The current research likely used a specific CKD dataset. Testing the model on diverse and more extensive datasets from different sources, demographics, and clinical settings is essential to ensure that the model performs consistently and robustly in real-world scenarios. Also, we need to develop methods to visualize and understand the features that the model uses for diagnosis.

References

1. Akter, S., Habib, A., Islam, M. A., Hossen, M. S., Fahim, W. A., Sarkar, P. R., Ahmed, M. Comprehensive Performance Assessment of Deep Learning Models in Early Prediction and Risk Identification of Chronic Kidney Disease. IEEE Access, 2021, 9, 165184-165206. https://doi.org/10.1109/ACCESS.2021.3129491

2. Bueno, G., Fernandez-Carrobles, M. M., Gonzalez-Lopez, L., Deniz, O. Glomerulosclerosis Identification in Whole Slide Images Using Semantic Segmentation. Computer Methods and Programs in Biomedicine, 2020, 184, 105273. https://doi.org/10.1016/j.cmpb.2019.105273

3. Bukowy, J. D., Dayton, A., Cloutier, D., Manis, A. D., Staruschenko, A., Lombard, J. H., Solberg Woods, L. C., Beard, D. A., Cowley, A. W. Jr. Region-Based Convolutional Neural Nets for Localization of Glomeruli in Trichrome-Stained Whole Kidney Sections. Journal of the American Society of Nephrology, 2018, 29(8), 2081-2088. https://doi.org/10.1681/ASN.2017111210

4. Chittora, P., Chaurasia, S., Chakrabarti, P., Kumawat, G., Chakrabarti, T., Leonowicz, Z., Jasiński, M., Jasiński, L., Gono, R., Jasińska, E., Bolshev, V. Prediction of Chronic Kidney Disease - A Machine Learning Perspective. IEEE Access, 2021, 9, 17312-17334. https://doi.org/10.1109/ACCESS.2021.3053763

5. Chowdhury, N. H., Reaz, M. B. I., Haque, F., Ahmad, S., Ali, S. H. M., A Bakar, A. A., Bhuiyan, M. A. S. Performance Analysis of Conventional Machine Learning Algorithms for Identification of Chronic Kidney Disease in Type 1 Diabetes Mellitus Patients. Diagnostics (Basel), 2021, 11(12), 2267. https://doi.org/10.3390/diagnostics11122267

6. Chowdhury, N. H., Reaz, M. B. I., Ali, S. H. M., Ahmad, S., Crespo, M. L., Cicuttin, A., Haque, F., Bakar, A. A. A., Bhuiyan, M. A. S. Nomogram-Based Chronic Kidney Disease Prediction Model for Type 1 Diabetes Mellitus Patients Using Routine Pathological Data. Journal of Personalized Medicine, 2022, 12(9), 1507. https://doi.org/10.3390/jpm12091507

7. Dritsas, E., Trigka, M. Machine Learning Techniques for Chronic Kidney Disease Risk Prediction. Big Data and Cognitive Computing, 2022, 6(3), 98. https://doi.org/10.3390/bdcc6030098

8. Ebiaredoh-Mienye, S. A., Swart, T. G., Esenogho, E., Mienye, I. D. A Machine Learning Method with Filter-Based Feature Selection for Improved Prediction of Chronic Kidney Disease. Bioengineering (Basel), 2022, 9(8), 350. https://doi.org/10.3390/bioengineering9080350

9. Ginley, B., Lutnick, B., Jen, K. Y., Fogo, A. B., Jain, S., Rosenberg, A., Walavalkar, V., Wilding, G., Tomaszewski, J. E., Yacoub, R., Rossi, G. M., Sarder, P. Computational Segmentation and Classification of Diabetic Glomerulosclerosis. Journal of the American Society of Nephrology, 2019, 30(10), 1953-1967. https://doi.org/10.1681/ASN.2018121259

10. Hermsen, M., de Bel, T., den Boer, M., Steenbergen, E. J., Kers, J., Florquin, S., Roelofs, J. J. T. H., Stegall, M. D., Alexander, M. P., Smith, B. H., Smeets, B., Hilbrands, L. B., van der Laak, J. A. W. M. Deep Learning-Based Histopathologic Assessment of Kidney Tissue. Journal of the American Society of Nephrology, 2019, 30(10), 1968-1979. https://doi.org/10.1681/ASN.2019020144

11. Hosseinzadeh, M., Koohpayehzadeh, J., Bali, A. O., Asghari, P., Souri, A., Mazaherinezhad, A., Bohlouli, M., Rawassizadeh, R. A Diagnostic Prediction Model for Chronic Kidney Disease in Internet of Things Platform. Multimedia Tools Applications, 2021, 80, 16933-16950 https://doi.org/10.1007/s11042-020-09049-4

12. Iftikhar, H., Khan, M., Khan, Z., Khan, F., Alshanbari, H. M., Ahmad, Z. A Comparative Analysis of Machine Learning Models: A Case Study in Predicting Chronic Kidney Disease. Sustainability, 2023, 15(3), 2754. https://doi.org/10.3390/su15032754

13. Islam, M. A., Majumder, M. Z. H., Hussein, M. A. Chronic Kidney Disease Prediction Based on Machine Learning Algorithms. Journal of Pathology Informatics, 2023, 14, 100189. https://doi.org/10.1016/j.jpi.2023.100189

14. Islam, M. A., Akter, S., Hossen, M. S., Keya, S. A., Tisha, S. A., Hossain, S. Risk Factor Prediction of Chronic Kidney Disease Based on Machine Learning Algorithms. 2020 3rd International Conference on Intelligent Sustainable Systems (ICISS), Thoothukudi, India, 2020, 952-957, https://doi.org/10.1109/ICISS49785.2020.9315878

15. Kumar, S., Parthasarathi, P., Hogo, M. A., Masud, M., Al-Amri, J. F., Abouhawwash, M. Breast Cancer Detection Using Breastnet-18 Augmentation with Fine-Tuned VGG-16, Intelligent Automation & Soft Computing, 2023, 36(2), 2363-2378, https://doi.org/10.32604/iasc.2023.033800

16. Lee, C. L., Liu, W. J., Tsai, S. F. Development and Validation of an Insulin Resistance Model for a Population with Chronic Kidney Disease Using a Machine Learning Approach. Nutrients, 2022, 14, 2832. https://doi.org/10.3390/nu14142832

17. Lee, J., Warner, E., Shaikhouni, S. et al. Unsupervised Machine Learning for Identifying Important Visual Features Through Bag-of-Words Using Histopathology Data from Chronic Kidney Disease. Scientific Reports, 2022, 12, 4832. https://doi.org/10.1038/s41598-022-08974-8

18. Lee, K. H., Chu, Y. C., Tsai, M. T., Tseng, W. C., Lin, Y. P., Ou, S. M., Tarng, D. C. Artificial Intelligence for Risk Prediction of End-Stage Renal Disease in Sepsis Survivors with Chronic Kidney Disease. Biomedicines, 2022, 10(3), 546. https://doi.org/10.3390/biomedicines10030546

19. Ma, F., Tao, S., Lingyu, L., Hongyu, J. Detection and Diagnosis of Chronic Kidney Disease Using Deep Learning-Based Heterogeneous Modified Artificial Neural

Network. Future Generation Computer Systems, 2020, 111, 17-26, https://doi.org/10.1016/j.future.2020.04.036

20. Sanmarchi, F., Fanconi, C., Golinelli, D., Gori, D., Hernandez-Boussard, T., Capodici, A. Predict, Diagnose, and Treat Chronic Kidney Disease with Machine Learning: A Systematic Literature Review. Journal of Nephrology, 2023, 36, 1101-1117. https://doi.org/10.1007/s40620-023-01573-4
21. Sawhney, R., Aabh, M., Shilp, S., Vipu, N. A Comparative Assessment of Artificial Intelligence Models Used for Early Prediction and Evaluation of Chronic Kidney Disease. Decision Analytics Journal, 2023, 6, 100169. https://doi.org/10.1016/j.dajour.2023.100169
22. Schena, F. P., Anelli, V. W., Abbrescia, D. I., Di Noia, T. Prediction of Chronic Kidney Disease and Its Progression by Artificial Intelligence Algorithms. Journal of Nephrology, 2022, 35(8), 1953-1971. https://doi.org/10.1007/s40620-022-01302-3
23. Sheehan, S., Mawe, S., Cianciolo, R. E., Korstanje, R., Mahoney, J. M. Detection and Classification of Novel Renal Histologic Phenotypes Using Deep Neural Networks. The American Journal of Pathology, 2019, 189(9), 1786-1796. https://doi.org/10.1016/j.ajpath.2019.05.019
24. Shi, Y., Qin, P., Hongmin, L., Zhengqian, Z., Xinge, Y., Fischer, K., Furth, S. L., Tasian, G. E., Yon, F. Automatic Kidney Segmentation in Ultrasound Images Using Subsequent Boundary Distance Regression and Pixelwise Classification Networks. Medical Image Analysis, 2020, 60, 101602, ISSN 1361-8415, https://doi.org/10.1016/j.media.2019.101602
25. Silveira, A. C. M., Sobrinho, Á., Silva, L. D., Costa, E. dB., Pinheiro, M. E., Perkusich, A. Exploring Early Prediction of Chronic Kidney Disease Using Machine Learning Algorithms for Small and Imbalanced Datasets. Applied Sciences, 2022, 12(7), 3673. https://doi.org/10.3390/app12073673
26. Singh, V., Asari, V. K., Rajasekaran, R. A Deep Neural Network for Early Detection and Prediction of Chronic Kidney Disease. Diagnostics, 2022, 12(1), 116. https://doi.org/10.3390/diagnostics12010116
27. Singh, V., Jain, D., A Hybrid Parallel Classification Model for the Diagnosis of Chronic Kidney Disease. The International Journal of Interactive Multimedia and Artificial Intelligence, 2023, 8(6), 14-28 https://doi.org/10.9781/ijimai.2021.10.008
28. Swain, D., Mehta, U., Bhatt, A., Patel, H., Patel, K., Mehta, D., Acharya, B., Gerogiannis, V. C., Kanavos, A., Manika, S. A Robust Chronic Kidney Disease Classifier Using Machine Learning. Electronics, 2023, 12(1), 212. https://doi.org/10.3390/electronics12010212
29. Tangri, N., Ferguson, T. W. Role of Artificial Intelligence in the Diagnosis and Management of Kidney Disease: Applications to Chronic Kidney Disease and Acute Kidney Injury. Current Opinion in Nephrology and Hypertension, 2022, 31(3), 283-287. https://doi.org/10.1097/MNH.0000000000000787
30. Venkatesan, V. K., Ramakrishna, M. T., Izonin, I., Tkachenko, R., Havryliuk, M. Efficient Data Preprocessing with Ensemble Machine Learning Technique for the Early Detection of Chronic Kidney Disease. Applied Sciences, 2023, 13(5). 2885. https://doi.org/10.3390/app13052885
31. Wang, W., Chakraborty, G., Chakraborty, B. Predicting the Risk of Chronic Kidney Disease (CKD) Using Machine Learning Algorithm. Applied Sciences, 2021, 11(1), 202. https://doi.org/10.3390/app11010202
32. Yan, X., Li, X., Lu, Y., Ma, D., Mou, S., Cheng, Z., Ding, Y., Yan, B., Zhang, X., Hu, G. Establishment and Evaluation of Artificial Intelligence-Based Prediction Models for Chronic Kidney Disease Under the Background of Big Data. Evidence-Based Complementary and Alternative Medicine, 2022, 2022, 6561721. https://doi.org/10.1155/2022/6561721
33. Zhou, Y., Yu, Z., Liu, L., Wei, L., Zhao, L., Huang, L., Wang, L., Sun, S. Construction and Evaluation of an Integrated Predictive Model for Chronic Kidney Disease Based on the Random Forest and Artificial Neural Network Approaches. Biochemical and Biophysical Research Communications, 2022, 603, 21-28. https://doi.org/10.1016/j.bbrc.2022.02.099